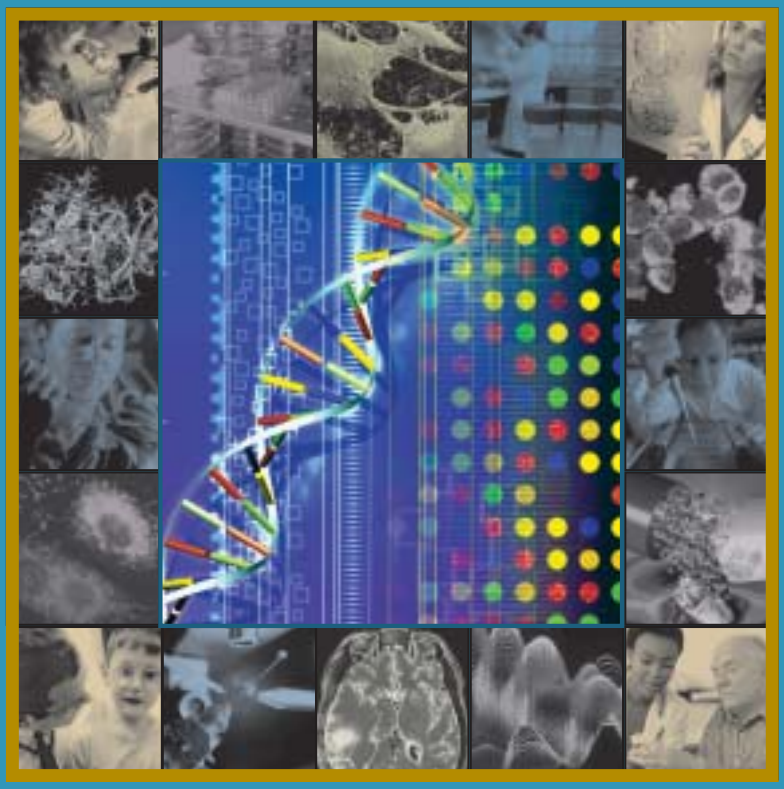
THE NATIONAL ADVANCED TECHNOLOGIES INITIATIVE FOR CANCER

Harnessing the Full Potential of Advanced Technologies To Eliminate Suffering and Death Due to Cancer

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • NATIONAL INSTITUTES OF HEALTH • NATIONAL CANCER INSTITUTE



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Introduction

When the National Cancer Act was signed in 1971, our Nation began a journey to defeat cancer. The destination has not been reached, but the journey has led to unimagined progress in our understanding of cancer as a disease process at the genetic, molecular, and cellular levels. Progress thus far has provided an ever-clearer perspective of the next phase of our journey. The major milestone in this phase will be the successful preemption of cancer, and it will be reached by improving our ability to prevent, detect early, and successfully eliminate many cancers and effectively manage other cancers as chronic diseases. Achieving this goal will allow us to eliminate the worst aspects of cancer, the suffering and death that it causes.

To eliminate the suffering and death due to cancer by 2015.

Experience over the past decade has shown that the most direct path to meet this challenge is through the optimal integration of science and technology. Our Nation's past successes in creating technologies to enhance scientific discovery — from the space program to the Human Genome Project — have produced dramatic scientific breakthroughs and advances. Now we have an opportunity to achieve an equally unimagined goal: to eliminate suffering and death due to cancer.

This goal is feasible because the recent unprecedented pace of discovery in basic biomedical science has provided an ever-increasing understanding of the mechanisms underlying cancer and other disease processes. Specific molecular and cellular changes in biochemical pathways have been identified that contribute to the initiation, progression and metastasis of cancer. We are currently in the process of harvesting this invaluable knowledge to preempt the process of cancer initiation and progression — a strategy that results in lives saved.

Our technologies and tools are sophisticated beyond the imagination of scientific pioneers of the past. Einstein's chalk and blackboard have been replaced by powerful computers, sophisticated analytic software, and networking that enables collaboration on a global scale. Information technologies and other advanced technologies such as genetic and protein microarray analysis, molecular imaging, and high throughput screening have helped us identify many of the complex mechanisms responsible for cancer and are proving themselves to be pivotal in accelerating our ability to intervene against these processes. *This point cannot be overemphasized: our ability to make rapid gains against cancer is intimately linked to the development and availability of advanced technologies that enable accelerated research and create effective interventions.*

The genomic and proteomic "revolutions" are already allowing us to detect cancer earlier, make more accurate diagnoses, and consequently make better treatment decisions. These advances depend on technologies that were not available to researchers or clinicians in the past. Similarly, technology-dependent, molecularly targeted therapies based on a patient's disease-

specific profile of markers provide hope that the cancer burden can be decreased and patients will enjoy a higher quality of life.

Consider the following examples:

- We know that an individual's genetic makeup, lifestyle, and exposure to environmental factors all influence cancer risk; the lack of individualized risk information has hampered the development of successful prevention strategies. Advanced genomic technologies, including high throughput screening and bioinformatics, are now allowing us to identify genetic variations that make certain individuals more vulnerable to specific environmental carcinogens. Further development of these approaches promises to yield effective medical and public health cancer prevention strategies.

- Detecting cancer before metastasis has occurred dramatically increases the odds of surviving the disease, but currently many cancers are first detected at advanced stages. Ovarian cancer is a clear case in point. When ovarian cancer is detected and treated early, the success rate is better than 95%, but currently more than 80% of these cases are detected at a late stage when the survival rate is less than 40%. By integrating our current understanding of carcinogenesis with innovative advanced technologies including laser-capture microdissection, protein arrays, and laser desorption and ionization, NCI scientists recently developed a blood test that improves the detection of ovarian cancer at an early stage. This test, if validated in future studies, will significantly improve the early detection and effective treatment of ovarian cancer as well as other cancers.

- One of the most vexing problems in oncology is that patients with the same form of cancer often respond differently to the same therapy. In the past few years, the use of advanced technologies has shown that cancer is comprised of molecularly distinct diseases that may require different treatment approaches. Through the customization of a cDNA microarray "lymphochip," researchers recently demonstrated that a cancer previously considered to be a single form of lymphoma is, in fact, two distinct diseases — only one of which responds well to the current standard therapy. Further refinement of this technology promises to accelerate the molecular classifications of all cancers and the development of more effective treatments.

- Current non-targeted cancer therapies (i.e., chemotherapy and radiation) often create devastating side effects. Our ability to understand the basis of differences between normal and cancerous cells now provides us the opportunity to identify molecular pathways that can be selectively targeted for treatment. This understanding, combined with the use of advanced

high throughput screening technologies of chemical libraries, was used to develop Gleevec™, a highly effective therapy for chronic myelogenous leukemia that has only minimal side effects. The development of Gleevec™ provided the proof of concept for highly effective molecularly targeted therapies.

We currently stand at a strategic inflection point, where transformative advances in technology could lead to rapid acceleration of biomedical research — and unprecedented progress against cancer. This extraordinary opportunity exists because of the convergence of a number of scientific discoveries, including completion of the sequencing of the human genome and the tremendous progress made in our understanding of the biology of normal and cancerous cells. To seize this opportunity, we must make a national effort to better integrate advanced technology development and deployment with cancer research and patient care.

This national effort must be driven by new approaches in the way science is done and through the convergence of scientific disciplines with enabling technologies. Interdisciplinary research teams composed of biologists, chemists, clinicians, physicists, mathematicians, materials scientists, and bioengineers must be assembled to create new ideas and solutions. New mechanisms must be created that enable the exchange of ideas and materials in unencumbered ways. The research and patient care advances developed by these teams of scientists and technologists must be rapidly and broadly disseminated throughout the cancer research and cancer care communities.

The National Cancer Institute (NCI) is committed to leading this effort by creating the National Advanced Technologies Initiative for Cancer, an unprecedented effort to develop and harness advanced technologies and optimize their integration into cancer research and cancer care. The initiative will complement and facilitate many aspects of the NIH Roadmap for Medical Research by enabling new pathways to discovery and creating research teams for the future. Moreover, the clinical and technical advances gained through this initiative will translate into progress against many serious diseases and improved health for all Americans and the world.

This document describes the NCI planning process for this initiative and provides some draft design concepts to illustrate potential directions.

Planning the Initiative

The planning for this initiative began in late Fall 2002 and continues to the present. The preliminary planning was largely conducted within NCI. Elements of the planning included a series of scientific focus working groups on molecular targets, systems biology, preclinical models, intracellular and *in vivo* imaging, clinical proteomics, and nanotechnology. Preliminary concepts for the overall initiative were presented to the NIH Director, other NIH Institute and Center Directors, and senior Department of Health and Human Services (DHHS) officials. These individuals provided feedback on the concept and suggested potential models for implementation.

The second phase of planning is being conducted with oversight and direction from the National Cancer Advisory Board (NCAB). It involves rapidly gathering input from a large and diverse group of experts in the broad cancer community to identify current and developing technologies that could significantly accelerate progress in selected areas of biomedical research. To that end, the NCAB, under the direction of the Chair, Dr. John Neiderhuber, has commissioned an *ad hoc* subcommittee to advise the NCI Director and the senior leadership team.

Specifically, the purpose of the *ad hoc* NCAB subcommittee is to:

- Conduct a needs analysis by exploring the potential contribution of current technologies in "cancer preemption." For example, what technology development and applications are needed to facilitate research and development in the areas of prevention, detection, prediction, elimination, or modulation of the process of cancer susceptibility, malignant transformation, tumor growth, invasion, metastasis, and acquisition of a lethal phenotype? What technologies are needed to facilitate our understanding and management of the cancer process in cells, tissues, individuals, and populations?

- Conduct an opportunities analysis of new and emerging technologies, such as nanotechnology and information technologies, and their potential application to biomedical research. What advanced developments and applications of technologies, in other fields or supported by other disciplines, could be applied to biomedical research?

- Consider possible models for technology development and how they might be integrated within a national network. The models could include an NCI intramural component, a number of extramural centers, consortia or collaborations, and individual awards for technology innovation. Input is requested with regard to how components would provide distinctive "added value" through their content; how they might be integrated; how they would be connected to the "Discovery-Development-Delivery" continuum; and how NCI would ensure that they maintain the highest quality.

- Consider how an initiative should relate to research on other diseases and to the other Institutes and Centers at NIH, other agencies of DHHS, or other Federal and state programs as well as academic centers.

The NCAB subcommittee will function through a task force of outside experts who will rapidly initiate and execute a process by which input can be consolidated from a broad cross-section of the community. Co-chaired by Drs. Eric Lander and Lee Hartwell, the task force will be composed of members from the cancer and the technology development communities. Task force members from the respective communities will co-lead a set of focus groups to identify specific opportunities and offer suggestions for how to realize them in the most timely manner. This strategy of widening circles of input is intended to rapidly and effectively gather insight and direct the development of the initiative.

The task force is expected to submit an interim report to the NCAB and NCI in six months. Concurrently, NCI is soliciting input through other mechanisms and is moving ahead with NCI, NIH, and DHHS procedures necessary to develop the initiative. In addition the NCI will convene other workshops and symposia to define the available resources and opportunities for the development and commercialization of enabling technologies.

Preliminary Concepts to Illustrate Potential Directions

As currently envisioned, this initiative will develop a coordinated national infrastructure to create new advanced biomedical technologies, provide training that facilitates interdisciplinary collaboration, and offer exceptional opportunities to integrate advanced technologies into biomedical research. It will be supported in part by existing NCI programs that develop and/or deploy enabling technologies for cancer research, especially multidisciplinary team research.

Structure of the Initiative

Several scenarios are possible. For example, the initiative could be created in a "hubs and nodes" configuration, with distributed components working together through an integrated network. In this scenario, "hubs" of scientific or technical expertise could be formed, providing selected unique technologies and capabilities to investigators across the nationwide biomedical research community. The "nodes" could provide excellence in specific technologies and/or unique capabilities in solving specific, multidisciplinary research problems. Connectivity, provision of cancer platforms, and coordination of the components, management structures, and policies would be administered by NCI. The network would have the capacity to link the most innovative biomedical scientists, clinicians, physical scientists, mathematicians, engineers, and others in cutting-edge collaborations with each other and with key partners in academia, the biotechnology and pharmaceutical industries, and other government agencies.

Areas of Focus

To date, through its preliminary planning efforts, NCI has identified five broad areas of potential focus for the initiative, including integrative computational biology and bioinformatics, advanced imaging, bioengineering and advanced prototyping, development and preclinical testing of prevention and therapeutic agents, and research resources.

Integrative Computational Biology and Bioinformatics. Development in these areas is needed to improve connectivity and synthesis of data among cancer researchers from all sectors. Specific needs in this critical area include data and image archiving and ultra-high capacity services to support complex analysis of vast amounts of genomic and proteomic data. The development of new analytical approaches is also needed, integrating progress made in commercial and government applications of computer science. Programs for advanced training in computation and other biomedical technology applications will be critical and necessary to bridge the divergent expertise needed for such large, multidisciplinary approaches.

Advanced Imaging. Advanced imaging programs will be critical in improving nearly all areas of cancer research, especially in the diagnosis of cancer and in monitoring the impact of cancer therapies *in vivo* in real time. As currently envisioned, a broad array of imaging modalities such

as high energy-force magnetic resonance imaging, nuclear imaging prototypes, positron emission tomography, optical imaging, ultrasonography, and others would become the focus of intense development. The integration of advanced imaging programs into existing research in cell cultures, small animal models, and clinical research would facilitate the development of molecular imaging reagents, dynamic assessment of cell function and interactions, and subcellular and macromolecular studies aimed at understanding functional interactions and fostering molecularly designed biopharmaceutical development.

Bioengineering and Advanced Prototyping. Bioengineering programs are needed to develop novel technological advances in areas such as nanotechnology and high throughput screening. Specific areas of research and development include material device construction, nanoscale fabrication, sensors development, and delivery systems. Facilities are needed to develop models and prototypes of these revolutionary diagnostic platforms to accelerate product development and dramatically enhance our ability to effectively detect cancer, deliver targeted therapeutics, and monitor the effectiveness of interventions.

Development and Preclinical Testing of Prevention and Therapeutic Agents. Programs are needed to enable the development and preclinical testing of new therapeutic and preventive agents. Comprehensive and rapid screening for molecular targets using biomarkers is critical to optimize chemical design and future testing modules. Chemical genomics programs are needed to establish libraries of new molecular entities, to support a range of activities including the identification of effector activities, and to establish safety profiles among combinations of molecules. A state-of-the-art biopharmaceutical development program, including Good Manufacturing Practices (cGMP) production facilities, would be needed to produce custom biopharmaceuticals for proof of principle clinical trials.

Research Resources. Research resources such as advanced animal models and biologic repositories are critical and must be available to the entire research community. Production of mouse models of disease and vivarium facilities are needed to provide all investigators with access to an extensive collection of highest quality genetically engineered mice. The archiving of tissue and other biospecimens is critically needed as a service to investigators throughout the cancer research community. Acquisition, archiving, and distribution functions for chemical libraries, biological compounds, and collections of natural products — a major strength of NCI — could also be provided as part of the national resource. High throughput screening and testing components serviced by robotics could be used to rapidly speed the identification of molecular targets.

Integration Throughout the Cancer Community

An integrated network of nationally distributed hubs and nodes could rapidly be established to support these and a wide range of other programmatic areas. Emphasis on innovation, translational application, commercialization, and bridging the gap between discovery and delivery will speed product development. Partnerships among academic and research institutes, the biotechnology and pharmaceutical industries, and other government agencies will be needed to catalyze and accelerate research and development in this new model. Most importantly, this initiative will create revolutionary new products to conquer disease and extraordinary opportunities to improve human health.

Conclusion

As conceived, the National Advanced Technologies Initiative for Cancer could serve as a foundation for cancer research in the 21st century by fostering the development and application of cutting-edge technologies to accelerate the discovery, development, and delivery research continuum. Active partners in the initiative will include scientists in the extramural academic and research institutes, biotechnology and pharmaceutical industries, and NCI and other government agencies. Moving decisively forward with this initiative will catalyze new diagnostic, prevention, and treatment strategies that will enable us to reach our 2015 Challenge Goal — the elimination of suffering and death due to cancer — for the benefit of every American and people the world over. Although this is an initiative led by the cancer research and care communities, it will benefit all in biomedical research and revolutionize healthcare.

Improvements in the care of cardiovascular disease, HIV/AIDS, and diabetes, to name just a few, are being driven by a similar scientific revolution. The development of advanced biomedical technologies will allow us to detect many diseases at the earliest stages and offer unique opportunities to translate advances in one disease quickly to another, capitalizing on the potential to develop new drugs directed at common pathways. NCI has a long history of partnerships with other NIH Institutes and Federal agencies and will lead and coordinate efforts to include them in this initiative.

The history of Federal investment in research at many of our Nation's premier research universities indicates that the initiative, both hubs and nodes, will likely create major opportunities for emerging and established companies in the biotechnology, pharmaceutical, and technology sectors. More importantly, however, the new products and services that arise from this alignment will accelerate our ability to conquer the major chronic diseases that plague mankind.

Our Nation's economy will almost certainly benefit from the initiative, as the global economy is increasingly being driven by knowledge-based industries including advanced biomedical technologies. In addition, a second, possibly even more powerful, economic stimulus effect will likely accrue. Improved care for cancer and other diseases based on molecularly targeted interventions will eliminate a vast portion of the human and financial loss associated with cancer and other diseases. Current estimates indicate that reducing the death rate from cancer by only 20% would contribute about $10 trillion to the Nation's economy, more than one year's gross national product.[1]

[1] K. Murphy and R. Topel (eds.) "Medical Care Output and Productivity," University of Chicago Press, 2002.

Determining how best to design and develop the National Advanced Technologies Initiative for Cancer requires input from experts throughout the technology and cancer research and care communities. NCI looks forward to receiving this input from the task force process and other sources and hopes that the entire community will participate in the design, implementation, and success of the initiative. It is clear that this initiative is a logical extension of existing successful pathways to progress. We have seen dramatic examples of "what can be" when we harness the power of advanced technologies in the areas of cancer prevention, early detection, diagnosis and therapeutics. We can and we must fully harness this potential now to successfully preempt cancer, save large numbers of lives, and increase the quality of life for many others. There is no more noble nor important goal.

We invite you to provide us with suggestions about the National Advanced Technologies Initiative for Cancer via email at the following address: NATICfeedback@mail.nih.gov.